Amendments to the Drawings:

The attached sheet of drawings includes changes to Fig. 8. This sheet replaces the original sheet including Fig. 8.

REMARKS/ARGUMENTS

Claims 24 to 38 are pending in this application. Claims 33 to 38 were withdrawn from further consideration by the examiner as being drawn to a non-elected invention. Claim 27 is amended herein. Basis for this amendments is found throughout the specification and claims as originally filed. No new matter has been added.

A replacement sheet for Fig. 8, which labels the protein memapsin 2 as having SEQ ID NO: 2, is attached after page 15.

ELECTION/RESTRICTION

The Action has required a restriction under 35 U.S.C. §121 to one of the following inventions:

1. Claims 24-32, drawn to a compound comprising a formula of claim 24 and a method for treating a patient to decrease the likelihood of developing or the progression of Alzheimer's disease by administering the compound thereof, classified in class 514, subclass 12; and
2. Claims 33-38, drawn to a method of preparing a Leu* Ala dipeptide isostere, classified in class 435, subclass 68.1.

Applicants hereby affirm the provisional election made with traverse to prosecute the invention of **Group 1, claims 24-32** made during the telephone conversation with Karen Dow on June 12, 2006.

OBJECTION TO THE SPECIFICATION AND DRAWING

As requested by the Action, the specification has been amended herein to update the continuity data of this application under the heading: "Related Applications" (e.g., the status of the parent application Serial No. 09/603,713 is identified).

A replacement sheet for Fig. 8, which labels the protein memapsin 2 as having SEQ ID NO: 2 is provided herein.

CLAIM REJECTION - 35 U.S.C. §112 1st PARAGRAPH

Compound Claims

The Action has rejected claims 24 to 32 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not reasonably provide enablement for a compound having a K_i of less than or equal to 1 nM for memepsin 2 as claimed in claim 27.

As amended herein, claim 27 is directed to the compound having structure of OM99-2, having a Ki of 1.6 nM for memepsin 2, which renders the rejection of this claim moot. Applicants respectfully request reconsideration and removal of this rejection.

Method Claims

The Action has rejected claims 24 to 32 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not provide enablement for methods of treating a patient to decrease the likelihood of developing or progressing Alzheimer's disease by administering to the individual an effective amount of the compound of claim 24, as set forth in claims 30 to 32. Applicants respectfully disagree.

As a preliminary matter, Applicants note that claims 24 to 29 are compound claims which do not involve any methods for treating diseases. The present §112, first paragraph rejection is therefore, inapplicable to these claims.

Applicants submit that method of treatment claims 30 to 32 are fully enabled by the specification, including decreasing the likelihood of developing or the progression of Alzheimer's disease. In particular, one of ordinary skill in the art, based on the teachings of the specification, could reasonably expect that the compounds of the invention function as claimed.

Much of Alzheimer's disease research has been focused on the amyloid cascade hypothesis, wherein amyloid β-42 (Aβ42), a proteolytic derivative of the large transmembrane protein amyloid precursor protein (APP), plays an early and crucial role. A major focus of research into Alzheimer's disease therapy involves blocking the production of Aβ42 by the specific inhibition of the key proteases required for Aβ42 generation. The identification of β-secretase (memapsin 2) as the aspartic protease that generates the N-terminus of Aβ42, has triggered the development of drug-like inhibitors of this enzyme, and has become one of the major targets for Alzheimer's disease (see, Citron, M., Trends in Pharmacological Sciences, pages 92-97, Vol. 25, No. 2, February 2004).

As discussed in the specification, Alzheimer's disease is degenerative disorder of the brain characterized by neutritic plaques. One of the principal constituents of these plaques is amyloid. Amyloid plaques are composed of polypeptide fibrils and are often present around blood vessels, reducing blood supply to various neurons in the brain (see, page 1, line 11 and lines 24 to 31 of the specification). APP is processed *in vivo* at three sites to afford amyloid (see, page 3, lines 27 to 31 and page 4, lines 1 to 4 of the specification). Cleavage of the β-secretase site (28 residues from the plasma membrane's luminal surface) and the β-secretase site (in the transmembrane region) results in the 40/42-residue β-amyloid peptide (Aβ), whose elevated production and accumulation in the brain are the central events in the pathogenesis of Alzheimer's disease. Memapsin 2 has been shown to be a β-secretase, a key protease involved in the production in the human brain of β-amyloid peptide from β-amyloid precursor protein (see, page 4, lines 23 to 24). Thus, one of ordinary skill in the art could reasonably conclude that a compound which inhibits β-secretase, i.e., memapsin 2, would be useful for treating and/or preventing Alzheimer's disease.

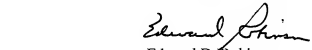
The compounds of the invention are capable of inhibiting β-secretase, i.e., memapsin 2, and therefore cleavage of APP caused by β-secretase (see, page 1, lines 8 to 10). Consequently, it is reasonable to conclude that the compounds of the invention are effective for treating a patient to decrease the likelihood of developing or the progression of Alzheimer's disease as set forth in claims 30 to 32. Applicants respectfully submit that the specification provides enablement for these claims and requests reconsideration and removal of this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6155.

Respectfully submitted,



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Attachments
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